

CLAIMS

What is claimed is:

1. A bone precursor composition, comprising

a calcium cement which is suitable for injection, wherein the calcium cement

- 5 includes monobasic calcium phosphate monohydrate and beta-tricalcium phosphate.

2. The composition of claim 1, further comprising calcium pyrophosphate and alpha-calcium sulfate hemihydrate.

3. The composition of claim 2, wherein the ratio by weight of monobasic calcium phosphate monohydrate to beta-tricalcium phosphate is 1:2 to 1:3.75 .

- 10 4. The composition of claim 1, wherein the calcium cement is in the form of granules with a diameter of between about 1 to 500 μm inclusive.

5. The composition of claim 4, which includes or is conditioned with cells.

6. The composition of claim 5, wherein the cells are tissue cells or mesenchymal cells.

- 15 7. The composition of claim 6, wherein the mesenchymal cells are connective tissue cells or bone cells.

8. The composition of claim 7, wherein the connective tissue cells are selected from the group consisting of ligament cells and chondrocytes and tendon cells.

9. The composition of claim 7, wherein the bone cells are selected from the group 20 consisting of bone marrow stem cells, osteocytes, osteoblasts and osteoclasts.

10. The composition of claim 1, further comprising an injection vehicle.

11. The composition of claim 10, wherein the injection vehicle is selected from the group consisting of microfibrillar collagen and unassembled liquid collagen.

- 25 12. The composition of claim 11, wherein said injection vehicle is unassembled liquid collagen in a concentration from about 0.5 mg/ml to about 40 mg/ml.

13. The composition of claim 10, wherein said injection vehicle further comprises collagen foam, collagen fiber particles, methyl cellulose, or a pharmaceutically acceptable vehicle.
14. The composition of claim 10, wherein said calcium cement comprises calcium pyrophosphate, alpha calcium sulfate hemihydrate, monobasic calcium phosphate monohydrate and beta tricalcium phosphate.
15. The composition of claim 2, wherein said calcium cement comprises, by weight, between about 1 and 5 percent calcium pyrophosphate, between about 5 and 15 percent alpha-calcium sulfate hemihydrate, between about 5 and 25 percent monobasic calcium phosphate monohydrate and between about 55 and 75 percent beta-tricalcium phosphate.
16. The composition of claim 1, further comprising a therapeutic or analgesic agent.
17. The composition of claim 11, wherein the collagen is fetal porcine collagen.
18. The composition of claim 1, further comprising macromolecules necessary for cell growth, morphogenesis, differentiation and tissue building.
19. The composition of claim 18, wherein the macromolecules are in the form of extracellular matrix particulates.
20. The composition of claim 19, wherein the extracellular matrix particulates comprise between about 0.05 to 20 weight percent of the composition when dry.
21. The composition of claim 1, further comprising pore-generating particles.
22. The composition of claim 21, wherein said pore-generating particles are selected from the group consisting of gelatin and calcium sulfate, or mixtures thereof
23. A bone precursor composite, comprising
a calcium cement; and
a biopolymer structure.
24. The composite of claim 23, wherein said biopolymer structure is collagen.
25. The composite of claim 24, wherein the collagen is fetal porcine collagen.

26. The composite of claim 23 wherein the biopolymer structure is a sponge or a single density foam.

Sub A 1 27. The composite of claim 23 wherein the biopolymer structure is a fiber or fibers.

28. The composite of claim 23 wherein the biopolymer structure is a matt.

5 29. The composite of claim 23 wherein the biopolymer structure is a double density foam.

Sub A 2 30. The composite of claim 23 wherein the biopolymer structure is a composite of a biopolymer structure and another structure.

10 31. The composite of claim 23, wherein the biopolymer foam and/or the calcium cement includes or is conditioned with cells.

32. The composite of claim 31, wherein said composition is mechanically conditioned.

15 33. A bone precursor composition, comprising a calcium cement; and acid or pepsin extracted collagen.

34. The composition of claim 33, wherein the collagen is in the form of lyophilized collagen.

35. The composition of claim 33, wherein the collagen is microfibrillar collagen.

20 36. The composition of claim 33, wherein the calcium cement includes calcium salts selected from the group consisting of calcium pyrophosphate, alpha-calcium sulfate hemihydrate, monobasic calcium phosphate monohydrate, beta-tricalcium phosphate, and mixtures thereof.

37. The composition of claim 34, wherein the collagen comprises between about 0.1 to 2.5 weight percent of the composition when dry.

25 38. The composition of claim 36, wherein the ratio by weight of monobasic calcium phosphate monohydrate to beta-tricalcium phosphate is 1:2.5 to 1:3.75.

39. The composition of claim 33, wherein the calcium cement is in the form of granules with a diameter of between about 1 to 500 µm inclusive.
40. A method for preparing an injectable bone precursor composition, comprising combining calcium pyrophosphate, alpha-calcium sulfate hemihydrate, monobasic calcium phosphate monohydrate and beta-tricalcium phosphate, such that an injectable bone precursor composition is prepared.
41. The method of claim 40, wherein the ratio by weight of monobasic calcium phosphate monohydrate to beta-tricalcium phosphate is 1:2.5 to 1:3.75.
42. The method of claim 40, further comprising the step of producing the bone precursor composition as granules of reacted, hardened cement having a diameter of between about 1 to 500 µm inclusive.
43. The method of claim 40, further comprising the step of contacting the bone precursor composition with a neutralizing solution such that a neutralized bone precursor composition is prepared.
44. The method of claim 43, wherein the neutralizing solution is selected from the group consisting of CAPS, triethanolamine, TES, tricine, HEPES, glycine, phosphate buffer solution, bis tris propane, TAPS, AMP and TRIS.
45. The method of claim 43, wherein the neutralizing solution is tribasic sodium phosphate.
46. A method for producing or repairing connective tissue in a subject, comprising administering an injectable bone precursor composition to the subject, wherein the injectable bone precursor composition comprises calcium pyrophosphate, calcium sulfate hemihydrate, monobasic calcium phosphate monohydrate and beta-tricalcium phosphate.
47. The method of claim 46, wherein the ratio by weight of monobasic calcium phosphate monohydrate to beta-tricalcium phosphate is 1:2 to 1:3.75.
48. The method of claim 46, wherein the bone precursor composition is in the form of granules with a diameter of between about 1 to 500 µm inclusive.

49. The method of claim 46, wherein the bone precursor composition includes or is conditioned with cells.
50. The method of claim 46, wherein the cells are tissue cells or mesenchymal cells.
51. The method of claim 46, wherein the bone precursor composition further comprises an injection vehicle.
52. The method of claim 46, wherein the bone precursor composition further comprises a biopolymer structure.
53. The method of claim 46, wherein the bone precursor composition further comprises a therapeutic and/or analgesic agent.
- 10 54. The method of claim 46, wherein the bone precursor composition further comprises acid or pepsin extracted collagen.
55. The method of claim 46, wherein the bone precursor composition further comprises extracellular matrix particulates.
- ✓ 56. The method of claim 46, wherein the bone precursor composition further
15 comprises pore-generating particles.